


Trends and outcomes of chronic coronary total occlusion–related ventricular tachyarrhythmias

Upenkumar Patel, MBBS, MPH^a, Mohammed Zubair, MD^a, Rezwan Munshi, MD^a , Rupak Desai, MBBS^b, and Amgad N. Makaryus, MD^{c,d}

^aDepartment of Internal Medicine, Nassau University Medical Center, East Meadow, New York; ^bDivision of Cardiology, Atlanta VA Medical Center, Decatur, Georgia; ^cDepartment of Cardiology, Nassau University Medical Center, East Meadow, New York; ^dDepartment of Cardiology, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell Health, Manhasset, New York

ABSTRACT

Our study aims to establish trends and frequencies of ventricular tachyarrhythmia (VTA) among patients with chronic coronary total occlusion (CCTO). We identified CCTO hospitalizations with and without VTA using the National Inpatient Sample. A total of 911,579 CCTO-related hospitalizations were identified, with 92,450 (10.1%) encounters associated with VTA. The CCTO-VTA cohort showed higher all-cause mortality (adjusted odds ratio [aOR] = 4.45, $P < 0.001$), longer hospital stays (6.8 vs 4.6 days; $P < 0.001$), and higher hospital charges (\$117,382 vs \$75,419; $P < 0.001$) compared to the CCTO non-VTA group. Rates and odds of cardiogenic shock (aOR = 4.19), venous thromboembolism (aOR = 2.09), respiratory failure (aOR = 2.85), and requirement of mechanical ventilation (aOR = 4.23) were higher in the CCTO-VTA group ($P < 0.001$). Over time, there was an increase in VTA (9.2% in 2010 to 12.1% in 2014) and all-cause mortality (7.5% in 2010 to 12.4% in 2014; $P < 0.001$). Trends in VTA among patients with CCTO increased by 4.8% for undergoing percutaneous coronary intervention and by 2.5% for undergoing both percutaneous coronary intervention and coronary artery bypass grafting ($P < 0.001$). Occurrence of VTA among CCTO patients is associated with worse outcomes and higher resource utilization.

KEYWORDS Chronic coronary total occlusion; coronary artery disease; ventricular tachyarrhythmias

Coronary total occlusion is defined as a complete obstruction of one or more coronary arteries leading to absence of antegrade blood flow or functional obstruction where there is minimal contrast penetration beyond the actual point of narrowing but without opacification of distal vessels on coronary angiography. A total occlusion that has been present for more than 3 months is considered a chronic coronary total occlusion (CCTO).¹ The actual prevalence of CCTO in the general population is unknown, though some studies have indicated a prevalence as high as 52%.^{1–6} The literature on the rates of ventricular tachyarrhythmias (VTA) in patients with CCTO compared to those without CCTO is disputable.^{7,8} In a meta-analysis by Chi et al there was a higher incidence of VTA and appropriate implantable cardioverter defibrillator therapy (1.68-fold) in patients with CCTO.⁹ Overall, data are lacking.

METHODS

The study cohort was acquired from the National Inpatient Sample data set (2007–2014). Institutional review board approval was not required for this study. The National Inpatient Sample is the largest publicly accessible health care database in the United States and comprises records of about 7 million unweighted and about 35 million weighted hospital encounters each year. Use of weighted data allowed us to measure national estimates.¹⁰

An *International Classification of Diseases, Ninth Revision* code was used to identify adult hospitalizations with known CCTO. We identified VTA as a codiagnosis of any rhythm disorders such as ventricular fibrillation, ventricular flutter, or ventricular tachycardia. These validated codes have been utilized in previously published studies during this period of analysis.¹¹ Discharges related to patients under the age of 18 were excluded from the study cohort.

Corresponding author: Amgad N. Makaryus, MD, Chairman, Department of Cardiology, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Nassau University Medical Center, 2201 Hempstead Turnpike, East Meadow, NY 11554 (e-mail: amakaryu@numc.edu)

The authors report no conflicts of interest.

Received March 5, 2021; Revised March 29, 2021; Accepted April 1, 2021.

Table 1. Baseline characteristics of ventricular tachyarrhythmias in hospitalized patients with chronic coronary total occlusion

Variable	CCTO – VTA	CCTO + VTA	P value
Weighted <i>N</i>	819,129	92,450	
Age (years) at admission			
Mean age ± SD	66.5 ± 12.1	66.1 ± 12.0	<0.001
18–44	3.9%	4.0%	<0.001
45–64	38.8%	39.5%	
≥65	57.3%	56.5%	
Sex			<0.001
Male	71.1%	80.4%	
Female	28.9%	19.6%	
Race			<0.001
White	78.2%	81.4%	
Black	8.6%	7.9%	
Hispanic	6.8%	5.2%	
Asian or Pacific Islander	2.1%	1.7%	
Native American	0.8%	0.6%	
Other	3.5%	3.2%	
Primary expected payer			<0.001
Medicare	58.7%	56.6%	
Medicaid	6.3%	6.0%	
Private including HMO	26.8%	28.7%	
Self-pay	4.8%	5.2%	
No charge	0.6%	0.5%	
Others	2.8%	3.1%	
Comorbidities			
Alcohol abuse	2.5%	3.7%	<0.001
Deficiency anemias	14.6%	15.2%	<0.001
RA/collagen vascular diseases	2.0%	1.7%	<0.001
Congestive heart failure	4.1%	4.6%	<0.001
Chronic pulmonary disease	21.4%	22.6%	<0.001
Coagulopathy	5.3%	8.6%	<0.001
Depression	7.5%	5.2%	<0.001
Uncomplicated diabetes mellitus	33.7%	27.4%	<0.001
Diabetes with chronic complications	7.4%	5.8%	<0.001
Drug abuse	1.8%	2.2%	<0.001
Hypertension	75.1%	66.6%	<0.001
Hypothyroidism	9.5%	8.1%	<0.001
Liver disease	1.3%	1.1%	<0.001
Fluid and electrolytes disorders	16.6%	28.2%	<0.001

(Continued on next column)

Table 1. Baseline characteristics of ventricular tachyarrhythmias in hospitalized patients with chronic coronary total occlusion (Continued)

Variable	CCTO – VTA	CCTO + VTA	P value
Peripheral vascular disorders	17.5%	16.4%	<0.001
Renal failure	18.1%	19.0%	<0.001
Valvular disease	1.7%	1.5%	<0.001

CCTO indicates chronic coronary total occlusion; HMO, health maintenance organization; RA, rheumatoid arthritis; VTA, ventricular tachyarrhythmias.

The Pearson chi-square test and Student's *t* test were utilized to assess categorical and continuous variables, respectively. The trends in the frequency of VTA in hospitalized CCTO patients were analyzed by the linear-by-linear association test. After adjusting for baseline characteristics and comorbidities, a two-step hierarchical multivariate regression model was used to measure the risk of hospitalization outcomes secondary to VTA in CCTO patients. IBM SPSS Version 22 was utilized for all statistical analyses.

RESULTS

A total of 911,579 CCTO-related hospitalizations were identified between 2007 and 2014. Of these, 92,450 (10.1%) encounters were associated with VTA (mean age 66.1 ± 12.0 years, 80.4% men, 81.4% white). Among CCTO-related hospitalizations, the frequency of VTA was highest in those aged ≥65 years (56.5%). The cohort with CCTO-VTA often consisted of Medicare enrollees (56.6%). Comorbidities such as alcohol abuse, anemia, chronic pulmonary disease, congestive heart failure, drug abuse, and fluid-electrolyte disorder were higher in the CCTO-VTA cohort than in the non-VTA cohort (*Table 1*).

The CCTO-VTA cohort showed worse hospitalization outcomes, including higher inpatient mortality (10.2% vs 2.0%; adjusted odds ratio [aOR] = 4.45; 95% confidence interval [CI], 4.16–4.75), longer hospital stays (6.8 ± 7.1 vs 4.6 ± 4.9 days), and higher hospital charges (\$117,382 vs \$75,419) compared to the cohort without VTA. The CCTO patients who experienced VTA were more likely to be transferred to short-term hospitals (4.3% vs 3.2%), skilled nursing facilities/intermediate care facilities, or other facilities (11.6% vs 8.5%) and more likely to receive home health care (12.8% vs 12.0%) than the non-VTA cohort. The cohort with VTA was less often routinely discharged from the hospital (60.5% vs 73.6%). Furthermore, other hospitalization outcomes including cardiogenic shock (14.9% vs 3.2%; aOR = 4.19; 95% CI, 3.96–4.42), venous thromboembolism (2.7% vs 1.1%; aOR = 2.09; 95% CI, 1.88–2.34), respiratory failure (24.3% vs 9.2%; aOR = 2.85; 95% CI, 2.73–2.97), and requirement for intubation/mechanical ventilation (21.9% vs 5.6%; aOR = 4.23; 95% CI, 4.05–4.44) were higher in the CCTO-VTA cohort than in the non-VTA cohort (*Table 2*).

Table 2. Outcomes of ventricular tachyarrhythmias in hospitalized patients with chronic complete total occlusions

Outcomes	CCTO – VTA	CCTO + VTA	P value	Adjusted odds ratio	95% CI (LL-UL)	Adjusted P value
All-cause in-hospital mortality	2.0%	10.2%	<0.001	4.45	4.16-4.75	<0.001
Venous thromboembolism	1.1%	2.7%	<0.001	2.09	1.88-2.34	<0.001
Respiratory failure	9.2%	24.3%	<0.001	2.85	2.73-2.97	<0.001
Cardiogenic shock	3.2%	14.9%	<0.001	4.19	3.96-4.42	<0.001
Intubation and mechanical ventilation	5.6%	21.9%	<0.001	4.23	4.05-4.44	<0.001
Disposition of patient			<0.001			
Routine	73.6%	60.5%				
Transfer to short-term hospital	3.2%	4.3%				
Other transfers (SNF, ICF, other facility)	8.5%	11.6%				
Home health care	12.0%	12.8%				
Against medical advice	0.5%	0.6%				
Total hospital charges (mean)	\$75,419	\$117,382	<0.001			
Length of stay (days) (mean ± SD)	4.6 ± 4.9	6.8 ± 7.1	<0.001			

CCTO indicates chronic coronary total occlusion; ICF, intermediate care facility; LL, lower level; SNF, skilled nursing facility; UL, upper level; VTA, ventricular tachyarrhythmias.

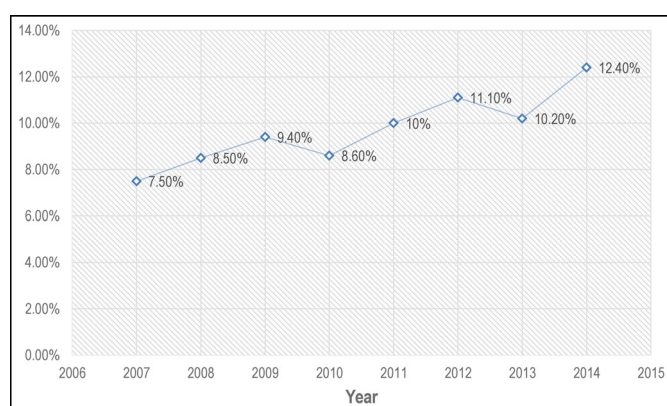


Figure 1. Trends of inpatient mortality among chronic total occlusion patients with ventricular tachyarrhythmias.

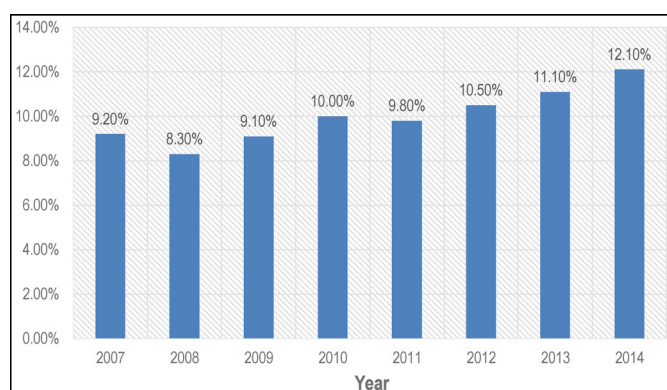


Figure 2. Trends in prevalence of ventricular tachyarrhythmias among chronic total occlusion patients.

There was an upwards trend of inpatient mortality among CCTO-VTA hospitalizations, from 7.5% in 2007 to 12.4% in 2014 (65.3% relative increase) (Figure 1). The frequency of

VTA in hospitalizations for CCTO also increased from 9.2% in 2010 to 12.1% in 2014 (31.5% relative increase) (Figure 2). Trends in VTA among CCTO-related hospitalizations increased by 4.8% in those who underwent percutaneous coronary intervention (PCI), whereas it increased by 2.5% in those who underwent both PCI and coronary artery bypass grafting (CABG). However, the frequency of VTA declined by 0.8% in CCTO patients who underwent CABG (Figure 3). All aforementioned data were statistically significant ($P < 0.001$).

DISCUSSION

Our study revealed that nearly 10% of hospitalized CCTO patients experienced VTA, resulting in poor outcomes (higher frequency and odds of all-cause mortality), prolonged hospital stays, and higher economic burden compared to those without VTA. Those with CCTO-VTA were more likely to develop complications such as cardiogenic shock, venous thromboembolism, respiratory failure, and the requirement for mechanical ventilation. There was an upwards trend in the frequency of VTA along with inpatient mortality in hospitalized CCTO patients who experienced VTA over the past few years. The rising trends of VTA were observed among CCTO patients who were treated with PCI and both PCI plus CABG. VTA with CCTO was observed more frequently in the elderly (aged ≥ 65). Our analysis also demonstrated an increased economic burden in the CCTO-VTA cohort due to outcomes that required additional postdischarge care and rehabilitation. Patients experiencing VTA had a prolonged hospital stay and consequent further deconditioning. In cases requiring electrical cardioversion, the experience could be traumatic and added to a delayed recovery.

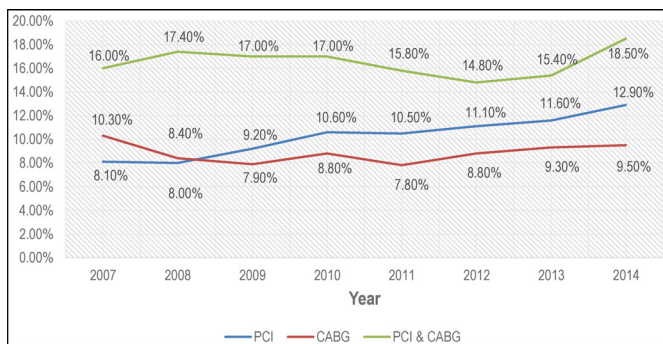


Figure 3. Trends of ventricular tachyarrhythmias in chronic total occlusion patients with percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and PCI and CABG.

There are numerous explanations for the generation of VTA in patients with CCTO. Reentry phenomenon, pro-arrhythmic properties of the ventricle with reduced ejection fraction, chronic hibernation of the affected myocardium, and heterogeneous sympathetic innervation could all contribute to the occurrence of VTA in this population.^{12–15}

Patients with CCTO should be thoroughly optimized using medical therapy. In addition to appropriate implantable cardioverter-defibrillator therapy to prevent sudden cardiac death, revascularization of the affected vessel can be considered to reduce the occurrence of VTA in CCTO patients. Most recent guiding principles identify ischemic symptom improvement as the primary indication for PCI in eligible CCTO groups.¹⁶ In one study, CCTO patients with reduced left ventricular ejection fraction ($\leq 35\%$) undergoing successful PCI experienced a significant increase in left ventricular ejection fraction at 6 months.¹⁷ Because low ejection fraction is assumed to be pro-arrhythmic, revascularization could reduce the frequency of VTA in these patients.¹³ In addition, revascularization can result in substrate normalization and myocardial stabilization, thereby reducing the frequency of VTA.

The rising trends in inpatient mortality in the CCTO-VTA cohort could be explained by proper classification, data gathering, and causal attribution. Limitations to this study include the administrative nature of the data set, diagnostic coding errors, inability to trace specific patient encounters longitudinally, and the possibility of overcalculation due to multiple inpatient admissions of the same patient. Closely matched groups could also help eliminate any underlying confounding factors. However, this is one of the largest nationally representative datasets available.

In conclusion, nearly 10% of hospitalized CCTO patients had VTA, and it was seen most frequently in elderly white men. The occurrence of VTA among hospitalized CCTO patients was associated with higher in-hospital mortality, cardiovascular complications, and health care resource utilization.

ORCID

Rezwan Munshi  <http://orcid.org/0000-0002-4472-775X>

1. Stone GW, Kandzari DE, Mehran R, et al. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: part I. *Circulation*. 2005;112:2364–2372. doi:10.1161/CIRCULATIONAHA.104.481283.
2. Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of chronic total coronary occlusion on treatment strategy. *Am J Cardiol*. 2005;95:1088–1091. doi:10.1016/j.amjcard.2004.12.065.
3. Fefer P, Knudtson ML, Cheema AN, et al. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions Registry. *J Am Coll Cardiol*. 2012;59:991–997. doi:10.1016/j.jacc.2011.12.007.
4. Jeroudi OM, Alomar ME, Michael TT, et al. Prevalence and management of coronary chronic total occlusions in a tertiary Veterans Affairs hospital. *Catheter Cardiovasc Interv*. 2014;84:637–643. doi:10.1002/ccd.25264.
5. Werner GS, Gitt AK, Zeymer U, et al. Chronic total coronary occlusions in patients with stable angina pectoris: impact on therapy and outcome in present day clinical practice. *Clin Res Cardiol*. 2009;98:435–441. doi:10.1007/s00392-009-0013-5.
6. Tsai TT, Stanislawski MA, Shunk KA, et al. Contemporary incidence, management, and long-term outcomes of percutaneous coronary interventions for chronic coronary artery total occlusions: insights from the VA CART program. *JACC Cardiovasc Interv*. 2017;10:866–875. doi:10.1016/j.jcin.2017.02.044.
7. Raja V, Wiegand P, Obel O, et al. Impact of chronic total occlusions and coronary revascularization on all-cause mortality and the incidence of ventricular arrhythmias in patients with ischemic cardiomyopathy. *Am J Cardiol*. 2015;116:1358–1362. doi:10.1016/j.amjcard.2015.07.057.
8. Labine L, Hildebrandt DA, Rutten-Ramos S, Lardy M, Claussen M, Burke MN. Impact of chronic total occlusions on mortality in patients presenting with cardiac arrest. *J Am Coll Cardiol*. 2013;62:B117. doi:10.1016/j.jacc.2013.08.1110.
9. Chi WK, Gong M, Bazoukis G, et al. Impact of coronary artery chronic total occlusion on arrhythmic and mortality outcomes: a systematic review and meta-analysis. *JACC Clin Electrophysiol*. 2018;4:1214–1223. doi:10.1016/j.jacep.2018.06.011.
10. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP). <https://www.ahrq.gov/data/hcup/index.html>. Accessed March 31, 2021.
11. Desai R, Kakumani K, Fong HK, et al. The burden of cardiac arrhythmias in sarcoidosis: a population-based inpatient analysis. *Ann Transl Med*. 2018;6:330–330. doi:10.21037/atm.2018.07.33.
12. Tse G, Yeo JM. Conduction abnormalities and ventricular arrhythmogenesis: the roles of sodium channels and gap junctions. *Int J Cardiol Heart Vasc*. 2015;9:75–82. doi:10.1016/j.ijcha.2015.10.003.
13. Buxton AE, Ellison KE, Lorvidhaya P, Ziv O. Left ventricular ejection fraction for sudden death risk stratification and guiding implantable cardioverter-defibrillators implantation. *J Cardiovasc Pharmacol*. 2010;55:450–455. doi:10.1097/FJC.0b013e3181d9f49c.
14. Sachdeva R, Agrawal M, Flynn SE, Werner GS, Uretsky BF. The myocardium supplied by a chronic total occlusion is a persistently ischemic zone. *Catheter Cardiovasc Interv*. 2014;83:9–16. doi:10.1002/ccd.25001.
15. Luisi AJ Jr, Fallavollita JA, Suzuki G, Canty JM Jr. Spatial inhomogeneity of sympathetic nerve function in hibernating myocardium. *Circulation*. 2002;106:779–781. doi:10.1161/01.CIR.0000028604.23202.AC.
16. Brilakis ES, Mashayekhi K, Tsuchikane E, et al. Guiding principles for chronic total occlusion percutaneous coronary intervention. *Circulation*. 2019;140:420–433. doi:10.1161/CIRCULATIONAHA.119.039797.
17. Galassi AR, Boukhris M, Toma A, et al. Percutaneous coronary intervention of chronic total occlusions in patients with low left ventricular ejection fraction. *JACC Cardiovasc Interv*. 2017;10:2158–2170. doi:10.1016/j.jcin.2017.06.058.